AMENDMENTS TO THE DRAWINGS

The two replacement sheets attached herewith include changes to Figs. 2 and 5. These two sheets, which include Figs. 2 and 5, respectively, serve to replace the original sheets, which included Figs. 2 and 5, respectively. Each figure was amended by inserting the following immediately below the graphs depicted therein: "The symbol '*' indicates that a statistically significant difference was observed." These amendments are fully supported by the specification as originally filed, e.g., at paragraph [0030]. No new matter has been added.

Attachments: Replacement Sheets

REMARKS/ARGUMENTS

Amendments to the Drawings

The Examiner is requested to approve the accompanying replacement drawings. As noted above, Figs. 2 and 5 have been amended to include statements that explain the meaning of the asterisks depicted therein. The amendments to the drawings are fully supported by the specification as originally filed, e.g., at paragraph [0030]. No new matter has been added.

Amendments to the Specification

Paragraphs [0033], [0035], [0041] and [0042] have been amended to include statements that explain the meaning of the asterisks depicted in the tables appearing on pages 8, 9 and 11 of the specification. The amendments to the specification are fully supported by the specification as originally filed, e.g., at paragraph [0030]. No new matter has been added.

Amendments to the Claims

Claim 1 has been amended to recite hearing loss at 4 kHz or 8 kHz. Claims 1 and 4-8 also have been amended by deleting the language "or a derivative thereof." Additionally, the claims have been amended to remove unnecessary language and/or to further clarify the subject matter recited therein. The claim amendments are fully supported by the specification as originally filed. No new matter has been added.

Office Action

The drawings have been objected to under 37 C.F.R. § 1.83(a) as allegedly failing to describe what the asterisks stand for.

The specification has been objected to as allegedly failing to describe the meaning of the asterisks depicted in the tables on pages 8, 9 and 11.

Claims 1 and 4-8 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Claim 1 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled.

Claims 1-8 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Nekrassov et al., *Brain Research, 868*, 222-229 (2000) ("Nekrassov et al.") in view of Hotz et al., *Eur. Arch. Otorhinolaryngol., 247*, 202-205 (1990) ("Hotz et al.").

Discussion of the Office Action

With regard to the drawings, as noted above, Figs. 2 and 5 have been amended to include statements, which explain the meaning of the asterisks depicted therein. To the extent that asterisks are not depicted in any of the remaining drawings (Figs. 1, 3, 4, 6 and 7), none of the remaining drawings are believed to be objected to. The amendment of Figs. 2 and 5 is therefore believed to render moot the objection to the drawings. Accordingly, withdrawal of the objection to the drawings and approval thereof are respectfully solicited.

With regard to the specification, as noted above, paragraphs [0033], [0035], [0041] and [0042] have been amended to include statements, which explain the meaning of the asterisks depicted in the tables appearing on pages 8, 9 and 11. The amendment of paragraphs [0033], [0035], [0041] and [0042] is believed to render moot the objection to the specification. Accordingly, withdrawal of the objection to the specification is respectfully solicited.

As to the rejection of claims 1 and 4-8, the Office has alleged that there is no written description for the effective treatment of hearing loss with *derivatives* of vinpocetine. As noted above, claims 1 and 4-8 have been amended to delete reference to vinpocetine derivatives. The amendment of claims 1 and 4-8 is believed to render moot the rejection as to the written description. Accordingly, withdrawal of the rejection as to the written description requirement is respectfully solicited.

In support of the rejection of claim 1, the Office has alleged that the specification is not enabling for "completely preventing hearing loss," but has admitted that Applicant's method is enabled for treating and preventing hearing loss associated with epilepsy at 4 and 8 kHz (Office Action, p. 7, last sentence). Applicant respectfully disagrees with the basis for the enablement rejection. Nevertheless, in an effort to advance prosecution of the subject application, and not in acquiescence of any rejection, claim 1 has been amended to recite hearing loss associated with epilepsy at 4 kHz or 8 kHz. The amendment of claim 1 is

believed to render moot the enablement rejection. Accordingly, withdrawal of the enablement rejection is respectfully solicited.

Regarding the obviousness rejection, Applicant respectfully submits that the cited references, alone or in combination, do not disclose or suggest whatsoever administering vinpocetine to treat hearing loss associated with epilepsy in the 4 kHz or 8 kHz range, e.g., as recited in claim 1. The cited references certainly do not disclose or suggest using vinpocetine to inhibit epileptic cortical activity in the ictal and post-ictal periods, e.g., as recited in claim 4. Indeed, the Office has admitted that Nekrassov et al. fails to teach treating hearing loss associated with epilepsy or any other symptom, e.g., cortical activity, associated with epilepsy (Office Action, p. 9, 2nd para.). Hotz et al. likewise fails to teach or suggest treating hearing loss associated with epilepsy.

Aminoglycosides have not been shown to change the physiology of the retro-cochlear nuclei generating the later ABR waves directly. Rather, aminoglycosides induce changes in the first wave of the ABR resulting from damage of the inner ear function. The aminoglycoside studies of Nekrassov et al. and Hotz et al. therefore invariably involve alterations in the most peripheral generators of the first wave of the ABR. While aminoglycoside-induced changes in the first wave may indirectly affect other ABR waves, the reverse is not true for ABR wave alterations associated with epilepsy, i.e., changes in the later ABR waves associated with epilepsy cannot indirectly change the first wave, which originates in peripheral structures. Indeed, not all ABR waves of such potentials originate from nuclei at the brainstem level.

Applicant is believed to be the first to report evidence that epilepsy alters the latency of the later ABR waves, i.e., retro-cochlear waves originating in brainstem nuclei of the auditory tract. See Nekrassov et al., *Epilepsy Research*, *53*, 245-254 (2003) ("Nekrassov et al. 2003"), a copy of which is attached for the Examiner's convenience. Nekrassov et al. 2003, published by the present inventors, is believed to disclose the first such reported evidence. Applicant's studies also have shown that the first wave (P1) of the ABR remain unchanged in ABR alterations associated with epilepsy (Nekrassov et al. 2003).

Applicant's invention provides a method for treating epilepsy-induced hearing loss with an acute vinpocetine pre-treatment. No such method is taught or suggested by any of the cited references, including Nekrassov et al., which discloses treating amikacin-induced hearing loss with a chronic (2 week) vinpocetine post-treatment regimen. Interestingly, Applicant's epilepsy studies initially were intended to study only the neuroprotective action of vinpocetine in a

manifestation of brain damage, e.g., as measured by EEG activity, and ABR was recorded as curiosity. Nevertheless, that curiosity led to Applicant's surprising and unexpected discovery of the presently claimed method, which now provides a promising treatment for epileptic patients. At the time of Applicant's invention, one of ordinary skill in the art, who was not aware of Applicant's discovery, simply would not have had any reasonable expectation that vinpocetine to could successfully prevent hearing loss associated with epilepsy as claimed herein. Such a result simply would not have been predictable in view of the cited references.

Applicant understands that a judgment on obviousness may involve some level of hindsight reasoning so long as it does not rely on knowledge gleaned only from an applicant's disclosure (M.P.E.P. § 2145(X)(*A*). However, "[d]etermination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 48 USPQ2d 1321 (Fed. Cir. 1998). Simply stated, "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Thus, the Office must not pick and choose from among isolated disclosures in the prior art to arrive at the claimed invention using the benefit of Applicant's disclosure as a guide. Indeed, there is no evidence that anyone prior to Applicant's discovery had heretofore discovered a method for treating or preventing hearing loss associated with epilepsy as recited in the instant claims. The cited art simply fails to disclose or suggest such a method.

Accordingly, Applicant respectfully submits that the amended claims are not obvious in view of the cited references. For at least the foregoing reasons, withdrawal of the obviousness rejection is respectfully solicited.

Conclusion

Applicant respectfully submits that the present application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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